Non-Technical Abstract

Chronic wounds of the lower extremity afflict more than 1% of the elderly population and a substantial percentage of those with diabetes. Our current treatments are not adequate. In fact, for our best therapies less than 60% of patients will heal after 5 months of care. Failure to successfully treat these wounds can lead to amputation, bone infection, social isolation, and depression. The psychologic devastation caused by a chronic wound includes the odor of rotting skin, pain, and the continual reminder of one's own mortality by the realization that a wound will not heal. The most common chronic wounds are called diabetic foot ulcers, venous leg ulcers, and pressure ulcers. The purpose of this project is to explore new therapies for two chronic wounds of the lower extremity that have distinct etiologies, the venous leg ulcer and the diabetic insensate foot ulcer.

Platelet derived growth factor (PDGF) is a protein that is involved in the early phases of wound repair. A topical version of PDGF was recently approved by the FDA for the treatment of diabetic neuropathic foot ulcer. After 5 months of care about 43% of patients who receive this treatment will heal. This is a 10% improvement over standard therapy (i.e., a 33% healing rate). This effect is dramatically less then would have been predicted from animal studies using PDGF. This effect has not been reproduced in other etiologically distinct chronic wounds, such as venous leg ulcer. Our belief is that the lack of efficacy of topically applied PDGF is related to its delivery to the wound bed.

In order to insure the delivery of PDGF to the wound, we plan to study the somatic gene transfer of PDGF to cells in the wound bed. In other words, we plan to have cells in the wound bed over-produce PDGF. This will be accomplished by using a replication deficient version of adenovirus (a version of the common cold virus). By using this technique, we expect that cells in the wound bed can be made to produce PDGF in large quantities. This will insure the presence of PDGF locally in the wound and hopefully improve the efficacy of this PDGF for the treatment of chronic wounds.